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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,084	05/24/2000	Keiya Ozawa	50026/012002	5150

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

HUNNICUTT, RACHEL KAPUST

ART UNIT PAPER NUMBER

1647

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/577,084

Applicant(s)

OZAWA ET AL.

Examiner

Rachel K. Hunnicutt

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-10 and 14-24 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 19 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10, 14 and 24 is/are allowed.
- 6) ☒ Claim(s) 1,4-8, 15-18, 20 and 23 is/are rejected.
- 7) ☒ Claim(s) 21 and 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0700, 1004, 1204.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

HC

RESPONSE TO AMENDMENT

Applicant's amendment filed November 29, 2004 is acknowledged. Claims 2, 10, and 12 have been canceled. Claims 1 and 10 are amended. Claims 1, 4-8, 10, 14-18, and 20-24 are under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Priority

There is no written support for the currently claimed invention in parent application 09/142,305. The '305 application does not mention fusion proteins comprising c-mpl. Therefore, the current application has a priority date as of its filing date which is May 24, 2000.

Information Disclosure Statement

In the correspondence mailed October 20, 2004, Applicants refer to supplemental information disclosure statements mailed on April 30, 2004 and June 22, 2004. The statement mailed on June 22, 2004 was acknowledged by the examiner and mailed to Applicants on July 27, 2004. The statement mailed on April 30, 2004 does not appear to be in the file. There is a statement that was mailed on April 16, 2004, and this statement was acknowledged by the examiner and mailed to Applicants on July 27, 2004.

Specification

The use of the trademark GENE PULSER™ (p. 16), RETRONECTIN™ (p. 22), PBLUESCRIPT™ (p. 29), and STEMPRO™ (p. 34) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections/Objections Withdrawn

The rejection of claims 1, 4-8, 10, 14-18, and 20 under 35 U.S.C. 112, first paragraph, for lack of enablement, is withdrawn in response to Applicants' amendment to the claims.

The rejection of claims 1, 4-8, 10, 14-18, and 20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicants' amendment to the claims.

The provisional rejection of claims 1, 4, and 23 under 35 U.S.C. 101 as claiming the same invention as that of claims 1 and 3 of copending Application No. 09/142,305, is withdrawn in response to Applicants' amendment to the claims.

The rejection of claim 2 under 35 U.S.C. 103(a) as being unpatentable over Gurney *et al.* in view of Wang *et al.* is withdrawn in response to Applicants' cancellation of the claim.

Claim Rejections/Objections Maintained and New Claim Rejections/Objections

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 8 and 18 recite "cell carrying the vector", which encompasses the host cell, as it occurs in nature, for example, as can be used for a gene therapy patient. However, since Applicants do not intend to claim a naturally occurring product, amendment of the claims to show the hand of man would obviate this rejection. It is suggested that claims 8 and 18 be amended to recite "an isolated cell" or a "purified cell" so long as there is support for the amendment in the specification. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 recites the limitation that the gene encoding a fusion protein and the exogenous gene are “located on separate molecules” in reference to the vector of claim 10. There is insufficient antecedent basis for this limitation in the claim. Claim 10 refers to a single vector encoding an exogenous gene and a fusion protein. All of the genes are contained within the same molecule, yet claim 17 refers to the genes being located on two different molecules. Claim 10 does not support the limitations found in claim 17.

Claims 5, 9, 15-17, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims all contain words or phrases in quotation marks, such as “ligand” and “ligand-binding domain”. By putting the words/phrases in quotation marks, there is an implication that a “ligand” is somehow different from a ligand. Is there an unspecified characteristic that distinguishes it from a ligand? The quotation marks are unnecessary and only serve to confuse the meaning of the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 4, 6-8, 20, and 23 under 35 U.S.C. 103(a) as being unpatentable over Gurney *et al.* in view of Wang *et al.* is maintained for reasons of record on p. 5-6 of paper no. 0704.

Applicants argue that there is nothing in the references that would provide any basis for selecting a steroid hormone receptor as a component of the claimed fusion proteins (p. 13 of response). Applicants argue that the examiner is basing her argument on an improper “obvious

to try” standard (p. 14 of response). Applicants also argue that the art does not suggest that a steroid hormone receptor, upon homodimerization, would function in combination with c-mpl in making a fusion protein as claimed (p. 14 and p. 16-17 of response)

Applicants’ arguments have been fully considered but have not been found to be persuasive. As stated in the previous office action, Gurney *et al.* used the growth hormone receptor (GHR) solely because of its homodimerization properties. Gurney *et al.* sought to characterize the proliferation activity of c-mpl, which must be in the dimer form in order for it to be active, so they engineered the GHR-c-mpl fusion protein which would dimerize c-mpl upon induction by GH. The statement quoted by Applicants regarding the “obvious to try” standard was taken out of context. Gurney *et al.* were trying to characterize c-mpl, and the point made in the argument was that any receptor known to form homodimers could be used in such experiments as performed by Gurney *et al.*

Regarding Applicants’ argument that one skilled in the art would not expect a steroid hormone receptor to dimerize and function in combination with c-mpl, it was known in the art at the time the application was filed that estrogen receptors were indeed useful in such fusion proteins. For example, Jackson *et al.* (1993, *EMBO J* 12(7): 2809-2819) teach a fusion protein comprising c-Abl and the estrogen receptor hormone binding domain. Jackson *et al.* teach that variants of several transcription factors were constructed by fusion to the hormone binding domains of the glucocorticoid receptor or the estrogen receptor, and the activity of the transcription factors could be controlled by hormones. Jackson *et al.* teach that a transforming derivative of c-abl becomes a hormone-inducible oncogene (p. 2809). Jackson *et al.* teach that using the hormone binding domain of the estrogen receptor is beneficial because its activation is relatively specific (p. 2817, column 1). Jackson *et al.* further teach that the strategy of engineering fusion proteins comprising the hormone binding domain of an estrogen receptor may provide regulable alleles for a variety of regulatory and enzymatic moieties, including gene products of unknown biochemical function (p. 2818). Jackson *et al.* refer to other tyrosine and serine kinases which could be regulated as estrogen receptor fusions. Thus, one skilled in the art would clearly expect the hormone binding domain of an estrogen receptor to be as useful as the growth hormone binding domain of GHR when fused to c-mpl. Applicants have not advanced

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the useful arts. Rather, they have substituted a receptor which was commonly engineered in fusion proteins wherein it was useful to have a partner which homodimerized.

Claims 1, 4, 6-8, 20, and 23 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Gurney *et al.* as applied to claims 1, 4, 6-8, 20, and 23 above, and further in view of Jackson *et al.* as discussed above. Gurney *et al.* teach a chimeric receptor comprising GHR fused to c-Mpl. Gurney *et al.* also teach that growth hormone induces homodimerization of the GHR, and homodimerization of c-Mpl is sufficient for receptor activation (p. 5296). However, Gurney *et al.* do not teach the use of an estrogen receptor instead of GHR.

Jackson *et al.* teach a fusion protein comprising c-Abl and the estrogen receptor hormone binding domain. Jackson *et al.* teach the benefits of using a specifically activated receptor that dimerizes as a fusion partner with proteins that need to form homodimers in order to be active. A person of ordinary skill in the art would have expected that the estrogen receptor as taught by Jackson *et al.* would be a useful substitution for the GHR as taught by Gurney *et al.* One skilled in the art would have been motivated to combine the teachings of Gurney *et al.* and Jackson *et al.* because both GHR and the estrogen receptor bind to specific ligands and can be easily regulated. They also both form homodimers, and they have both been shown to be useful when engineered as part of a fusion protein wherein the second protein is only active in dimer form. Accordingly, the invention taken as a whole is prima facie obvious over the prior art.

Conclusion

Claims 10, 14, and 24 are allowed.

Claims 21-22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1, 4-8, 15-18, 20, and 23 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
3/7/05


JANET ANDRIES
PRIMARY EXAMINER